ENABLING COMPETITION IN PHARMACEUTICAL MARKETS

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I. INTRODUCTION

The United States, unlike many other industrialized nations, does not regulate the price of pharmaceutical products directly. There are advantages to this approach. The U.S. generic market is one of the most dynamic and cost-effective in the world due to competition between manufacturers. The inventor of a socially valuable patented drug may charge high prices in the U.S. market, and the ensuing profit incentivizes innovation that benefits consumers. Subsequent competition between substitute therapies, even those on patent, can push down these prices over time. Generic entry after patent expiration pushes down prices even further. This form of price discipline, generated by market forces, rewards the attributes and efficacies that consumers want. For example, if a particular drug is differentiated from its competitors in a useful way, it will be able to command a higher price.

Prices that reflect value create exactly the incentives society desires for innovation. If the forces of competition are always strong, then the way for a pharmaceutical company to earn high profits is to invent a valuable treatment. If competitive forces weaken, then high prices for drugs may not reflect value but instead a lack of market discipline, sometimes exacerbated by regulations that enable or maintain high prices. When manufacturers can earn high profits by lobbying for regulations that weaken competition, or by developing mechanisms to sidestep competition, the system no longer incentivizes the invention of valuable drugs. Rather, it incentivizes firms to locate regulatory niches where they are safe from competition on the merits with rivals. The U.S. system performs well when competitive forces are strong, as this yields low prices for consumers as well as innovation that they value.

Weak competitive forces are more damaging to consumers in the pharmaceutical sector than some others. Patients in the U.S. are typically both insured and uninformed about therapeutic substitutes for the medications they take; thus, without effective rules and frameworks provided by the government, they face difficulty in creating market forces on their own. Without market pressures, drug makers may sell at arbitrarily high prices to insured consumers. Therefore, the policy environment in which those consumers shop is critical to maintaining effective price competition.

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Without a return to competitive conditions in this sector, expenditure will continue to grow. We are already hearing calls for regulation of pharmaceutical prices and seeing legislation that proposes price regulation.[1] It is very difficult to devise regulation that encourages innovation in a fast-changing industry. Regulators may be uninformed about valuable research, be captured by the industry, or lack the resources to keep up with changes in science or the cost of production.[2] Because innovation is hugely valuable to consumers, we are hesitant to recommend government regulation of pharmaceutical prices as a solution to the current problem of high and growing pharmaceutical expenditures.

The regulatory system in the U.S. is designed, in principle, to enable vigorous and effective competition that will bring down drug prices, particularly of any drug that faces a competitor or substitute. Over the last 10-15 years, however, industry participants have managed to disable many of these competitive mechanisms and create niches in which drugs can be sold with little to no competition. We argue in this paper that the first step toward bringing down pharmaceutical prices would simply be to fully apply the existing rules we already have. For example, speedy and effective entry of generic products, and financial incentives for consumers to choose treatments that have offered significant discounts are both part of the existing regulatory framework and result in lower prices. Both forces, however, have been greatly attenuated or stymied by the actions of pharmaceutical manufacturers. Enforcement of existing regulations that make markets more competitive will reduce pharmaceutical expenditures. The one type of market we will not address in this paper is the case of the patented, valuable medication that has no therapeutic substitutes because it represents a breakthrough in treatment. We refer the reader to the companion piece by Frank and Zeckhauser for a discussion of pricing when a drug faces no competition.[3] We note that industry participants who benefit from the status quo may work against a return to competitive markets. If pharmaceutical firms and other market participants block policies that restore competition, then calls for more stringent regulation will re-appear and may well be successful.

In this paper, we outline three major barriers to effective competition in U.S. pharmaceutical markets. The first focus of the paper is on biologics, the fastest growing segment of drug spending. This category has seen price increases in double digits for a decade and now (along with specialty drugs) represents more than one third of total spending with only increases in sight. Moreover, because the science behind biologic treatments is newer, regulations that would enhance competition in the sector are less well developed. In particular, regulatory delays have left the United States without competitive biosimilars – biologic entrants analogous to generics – that create price competition. There are only two biosimilars on the market in the U.S. while there are more than twenty on the market in the EU. This delay in biosimilar entrance in the U.S. carries a hefty price tag. We also outline regulatory barriers that are likely to inhibit biosimilar competition even after FDA approval. These barriers have also been used by brands to prevent entrance of traditional generics, and include pay for delay schemes, abuse of orphan drug classifications, and REMS requirements meant to increase drug safety. These barriers have also slowed the market response to price hikes in small generic markets. In conjunction with the FDA's slow progress on biosimilar approval, these tactics have led to a decline in the fraction of pharmaceutical expenditure exposed to significant price competition.

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1 On March 29, 2017, the Improving Access to Prescription Drugs Act was introduced in the Senate and the House, which, among other policy proposals, calls for Medicare to negotiate "fair prices" for prescription drugs, requires monitoring of price gouging by manufacturers, rebates from manufacturers to consumers, and shorter periods of marketing and data exclusivity for brand-name drugs. This legislation represents just the latest call for greater price regulation of drugs.

The second focus of the paper relates to the demand side imperfections of market participants. Pharmacy Benefit Managers (PBM), which are increasingly consolidated, may face agency problems that undermine their stated goal of bargaining for lower drug prices. PBMs may use rebates as a tool to increase profits by keeping a share of the high prices paid by patients who consume costly medication. Additionally, product hopping schemes instituted by brands and suboptimal Medicare reimbursement policies undermine patient incentives to substitute toward cheaper drugs. These problems are exacerbated by the ability of brands to provide kickbacks in the form of coupons, financial assistance, free meals, patient care, and other benefits designed to undo the financial incentives that exist in the marketplace and would otherwise steer demand to lower-priced alternatives. Insurers that negotiate low prices for a brand also give patients a low copay to steer them toward more cost-effective products, giving them higher market shares, but higher copays can be eliminated by competitors that provide financial assistance (e.g. coupons) to patients. These payments counteract the insurer's pricing incentives and lead the patient to consume the more expensive drug. In equilibrium, this results in higher prices on all drugs that consumers ultimately pay.

The third focus of this paper relates to older drug markets, where firms with small portfolios have recently instituted drastic price increases for essential drugs. This market also faces the potential for shortages and exit of competitors over time. After discussing these problems in some detail, we propose specific policies that would remedy or remove these barriers to competition, thereby lowering prices while incentivizing targeted innovation to the most valuable unmet medical needs.

II. MARKET TRENDS IN BIOLOGIC AND SPECIALTY DRUGS

Over the past two decades, pharmaceutical innovation has shifted from chemically-synthesized small molecule drugs toward more complex, bioengineered treatments grown from living tissue that are known as biologics. Biologics are often used to treat severe diseases that do not have effective small molecule treatments. The development of biologic medicines has represented a boon to many patients suffering from cancer, hepatitis, hemophilia, multiple sclerosis, autoimmune disorders such as rheumatoid arthritis, or inflammatory diseases such as Crohn's and ulcerative colitis. Many of these drugs impart high value to patients. Being able to sell at a high price while being protected from competition by a valid patent incentivizes manufacturers to innovate and produce high-value products. Recent hepatitis drugs, for example, have received negative press for the high prices that they carry, but they also represent some of the most innovative medical treatments in recent years, curing a disease that previously required a liver transplant. On other other hand, many drugs have high prices not justified by their value. This paper focuses on the incentives that enable the persistence of high prices when competing alternatives should drive down those prices.

The top thirty best-selling biologics, with licensure date, manufacturer, and corresponding indications, are listed in Table 1. Annual per-patient expenditure as measured by wholesale acquisition cost (WAC) demonstrates that biologics typically carry a high annual per-patient expenditure in the tens of thousands of dollars. Cheaper biologics, by this measure, tend to be insulins. Insulins are so widely used, however, that in aggregate, they are large contributors to pharmaceutical spending. Strikingly, although the biologics listed below carry a high price tag, many were licensed in the 1990s or early 2000s, suggesting that prices are high despite relevant patents having expired.

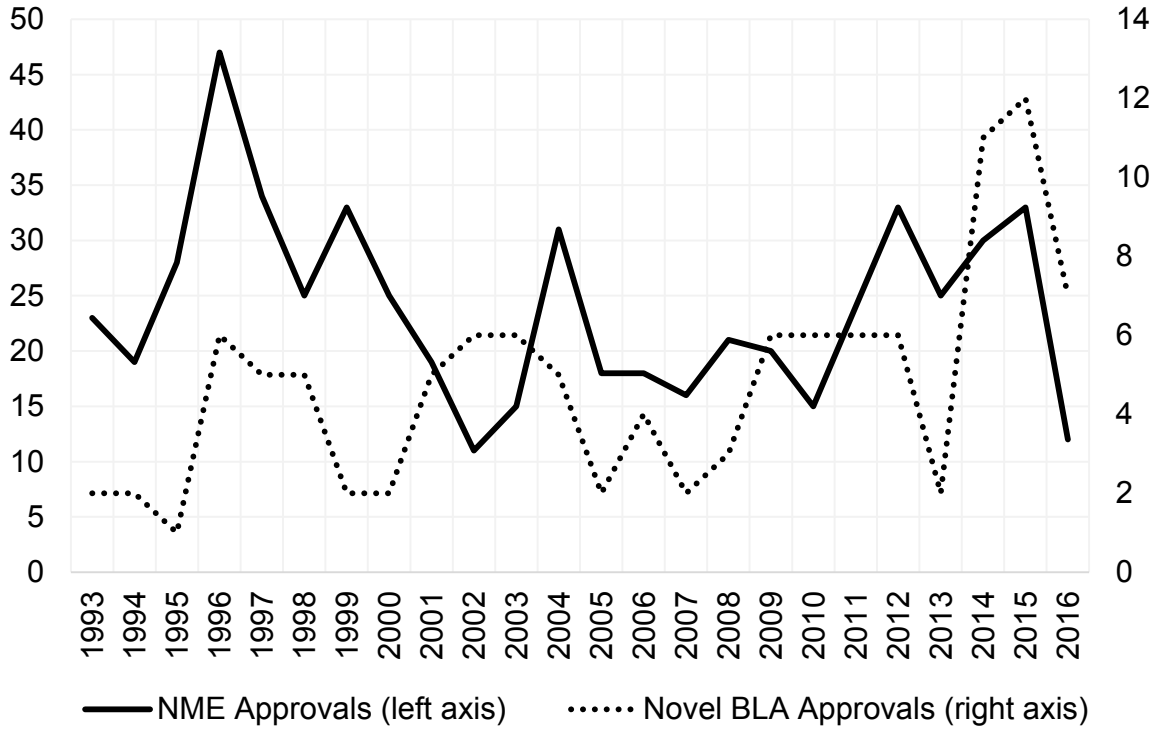
Table 1: Top 30 biologic drugs by sales

Proprietary name	Date of licensure	Innovator	2016 sales (US $billion)	WAC (Annual per patient expenditure)	Common indications
Humira	Dec-02	Abbvie Inc	11.7	$41,460 - $48,372	Rheumatoid Arthritis, Crohn's disease, Ulcerative colitis
Enbrel	Nov-98	Amgen Corporation	7.1	$41,468 - $51,835	Rheumatoid Arthritis
Remicade	Aug-98	Johnson & Johnson	5.2	$32,686	Rheumatoid Arthritis, Crohn's disease, Ulcerative colitis
Neulasta	Jan-02	Amgen Corporation	4.2	$19,659	Cancer
Rituxan	Nov-97	Hoffmann-la Roche	3.7	$29,916 - $38,142	Cancer, Rheumatoid Arthritis
Lantus	Apr-00	Sanofi Aventis	3.6	$2,982 - $4,473	Diabetes
Avastin	Feb-04	Hoffmann-la Roche	3.1	$91,572 - $124,908	Cancer, Macular Degeneration
Opdivo	Dec-14	Bristol meyer squibb	2.7	$30,090	Cancer
Herceptin	Sep-98	Hoffmann-la Roche	2.6	$50,201	Breast Cancer
Humalog	Jun-96	Lilly	2.2	$5,904	Diabetes
Stelara	Sep-09	Johnson & Johnson	2.2	$25,655 - $81,900	Psoriasis
Novolog	Jun-00	Novo Nordisk	2.1	$3,065	Diabetes
Tysabri	Nov-04	Biogen Idec Corp	1.9	$63,096	Crohn's Disease, Multiple Sclerosis
Epogen/Procrit	Jun-89	Amgen Corporation	1.7	$13,128 - $17,505	Anemia, Renal Failure, Cancer
Lucentis	Jun-06	Hoffmann-la Roche	1.5	$14,000 - $23,400	Macular Degeneration
Orencia	Dec-05	Bristol meyer squibb	1.5	$33,054 - $38,436	Rheumatoid Arthritis
Xolair	Jun-03	Hoffmann-la Roche	1.4	$10,488-$62,930	Rheumatoid Arthritis, Asthma
Aranesp	Sep-01	Amgen Corporation	1.1	-	Renal Failure
Perjeta	Jun-12	Hoffmann-la Roche	1.0	$55,046	Anemia, Renal Failure, Cancer
Xgeva	Jun-10	Amgen Corporation	1.0	$22,620	Osteoporosis, Bone Cancer
Avonex	May-96	Biogen Idec Corp	1.0	$64,032	Multiple Sclerosis
Levemir	Jun-05	Novo Nordisk	1.0	$3,228 - $4,842	Diabetes
Prolia	Jun-10	Amgen Corporation	0.9	$12,326	Osteoporosis, Bone Cancer
Simponi	Apr-09	Johnson & Johnson	0.9	$41,997 - $56,345	Rheumatoid Arthritis, Ulcerative Colitis
Cimzia	Apr-08	UCB	0.8	$39,563	Rheumatoid Arthritis, Crohn's disease
Neupogen	Feb-91	Amgen Corporation	0.7	-	Cancer, HIV/AIDS
Tarceva	Nov-04	Hoffmann-la Roche	0.7	$71,184 - $80,508	Cancer
Erbitux	Feb-04	Lilly	0.6	$138,861	Cancer
Synagis	Jun-98	Astrazeneca Corp	0.5	$35,571	Respiratory Syncytial Virus
Cosentyx	Jan-15	Novartis	0.4	$54,840	Plaque Psoriasis, Psoriatic Arthritis

Source: All data except for prices sourced from "2016-2020 Roadmap: $20 Bln Trophy with Pricing Challenge" (Morgan Stanley, November 14, 2016). Pricing data sourced from "High-Priced Drugs: Estimates of Annual Per-Patient Expenditures for 150 Specialty Medications," Report (AHIP, April 2016), https://www.ahip.org/wp-content/uploads/2016/04/HighPriceDrugsReport.pdf., and "Data Sample Shows January Brand Price Increases of ~6.2%, down ~180bps y/Y" (Leerink Partner LLC Equity Research, January 17, 2017). WAC data for Aranesp and Neupogen not available.

The shift toward biologic sales in the United States is reflected by corresponding growth in R&D spend in the biotech industry and biologic approvals by the FDA. Whereas traditional drugs must file for FDA approval via a New Drug Application (NDA), most biologic drugs undergo a separate regulatory approval process known as a biologic license application (BLA).[4] The growth in novel biologic license issuances compared to new molecular entities (NMEs), shown in Figure 1, demonstrates how the industry has shifted toward biologics, especially in recent years.

Figure 1: Biologic license approvals[5]



Source: John K. Jenkins, "CDER New Drug Review: 2016 Update," Presentation, (December 14, 2016), https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM533192.pdf.

BROOKINGS

In the United States, biologics have grown from just 13% of pharmaceutical spending in 2006 to 27% in 2016 as shown in Figure 2 below.[6]

Although total pharmaceutical spending has been increasing rapidly, with 29% cumulative growth between 2011 and 2015, utilization has remained roughly constant, with only a 1% increase in units sold over the same period.[7] This indicates that increased pharmaceutical spending can be attributed to increases in the price of the average bundle of drugs consumed, a shift caused both by price increases and consumption of more expensive drugs.

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4 Some biologic drugs, such as insulin, continue to follow the traditional regulatory pathway.
5 Data excludes BLA approvals that do not contain a new active ingredient.
6 These statistics include biologic insulins as well as biologics that have been approved via a Biologic License Approval. This may somewhat understate true biologic spending as it does not include some vaccines and hormones that are neither insulins nor approved with a BLA.
7 "Global Pharmaceuticals, US, China, Japan and Europe: The Grand Tour of Drug Pricing, Reform, and Market Growth," Report (UBS Global Research, February 9, 2017). W. Price, I. I. Nicholson, and Arti K. Rai, "Manufacturing Barriers to Biologics Competition and Innovation," Iowa L. Rev. 101 (2015): 1023.

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